DISSERTATION ON ELEVATED SERUM AMYLASE AND LIPASE LEVELS WITHOUT ACTUAL PANCREATIC INVOLVEMENT IN THE PRESENCE OF DKA – AN OBSERVATIONAL STUDY

Submitted in partial fulfilment of

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CERTIFICATE

This is to certify that the dissertation entitled**" ELEVATED SERUM AMYLASE AND LIPASE LEVELS WITHOUT ACTUAL PANCREATIC INVOLVEMENT IN THE PRESENCE OF DKA - AN OBSERVATIONAL STUDY**" is a bonafide work done by **DR.C.SANGESHWARAN** , post graduate student, Institute of Internal Medicine, Madras Medical College, Chennai-3 in partial fulfillment of the University Rules and Regulations for the award of MD Branch – I Internal Medicine, under our guidance and supervision, during the academic period from may 2010 to april 2013

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I solemnly declare that the dissertation entitled" **" ELEVATED SERUM AMYLASE AND LIPASE LEVELS WITHOUT ACTUAL PANCREATIC INVOLVEMENT IN THE PRESENCE OF DKA - AN OBSERVATIONAL STUDY** " is done by me at Madras Medical College, Chennai-3 during May2010 – April 2013 under the guidance and supervision of Prof.S.Tito M.D, to be submitted to The Tamilnadu Dr M.G.R Medical University towards the partial fulfillment of requirements for the award of M.D DEGREE IN GENERAL MEDICINE BRANCH-I.

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CONTENTS

INTRODUCTION

Diabetes mellitus is a group of disorders characterized by chronic hyperglycemia associated with disturbances of carbohydrate, protein, and fat metabolism, due to absolute or relative deficiency in insulin secretion and /or action.

Diabetes causes long term damage, dysfunction and failure of various organs especially the eyes, kidneys, nerves, heart and blood vessels.

There are two types of diabetes mellitus present.

Type-I DM - These patients depend on insulin for survival. There is autoimmune destruction of □ cells here.

Type 2-DM - impaired beta cell function with marked increase in peripheral insulin resistance and increased hepatic glucose output production.

In diabetic ketoacidosis, one of the hyperglycemic emergencies, there is insulin deficiency coupled with concomitant elevation of counter regulatory hormones. This hormonal imbalance promotes gluconeogenesis, glycolysis, glycogenolysis, protein breakdown and lipolysis.

The metabolic dearrangements of patients with DKA are hyperglycemia, metabolic acidosis, ketosis etc.

There are case reports, showing non specific elevation of serum amylase and lipase in patients with DKA, without actual pancreatic involvement.

The symptoms of DKA like nausea, vomiting, epigastric pain can be present in acute pancreatitis also.

Elevation of serum amylase, and lipase levels in association with severe abdominal pain often trigger the initial diagnosis of acute pancreatitis.

But in the presence of DKA, the patient may need CECT abdomen to diagnose acute pancreatitis.

So, it was decided to undertake a cross sectional study on the elevation of serum amylase and lipase in patients with DKA, and its relevance to the presence of acute pancreatitis, in the institute of internal medicine, Rajiv Gandhi Government General Hospital, Chennai.

AIMS AND OBJECTIVES

1. To measure the levels of serum amylase and lipase in patients with DKA
2. To Analyse whether elevated amylase and lipase levels can be present without actual pancreatic involvement in the presence of DKA
3. To identity the correlation between the elevation of serum amylase, lipase and morbidity, mortality of DKA
4. To identity the correlation between the elevation of serum amylase, lipase and variables like Na^+ ,K^+ ,HCo_3, Ph, urea, blood, sugar, serum osmolality, and types of DM.

REVIEW OF THE LITERATURE

DIABETIC KETO ACIDOSIS

Diabetic Keto acidosis remaining as a very serious medical condition and it leads to morbidity and mortality particularly in Patients with Type-1 diabetes mellitus and also in patients with type-2 diabetes mellitus to some extent.

In type 1 Diabetes mellitus, Diabetic keto acidosis can be the presenting manifestation at the starting itself. The presence of Type-1 diabetes mellitus may be diagnosed after the initial symptom complex of DKA in some cases.

But the Diabetic keto acidosis occurs usually in individuals already diagnosed to have diabetes mellitus.

Catobolic stress of trauma, surgery, infections, acute cerebrovascular accidents, myocardial infarctions lead to diabetic keto acidosis in patients with type 2 diabetes mellitus.

Auto immune type 1 diabetes leads to diabetic ketoacidosis when patient omits the insulin therapy.

After the introduction of insulin therapy, the mortality in DKA is less than 5% only.

Diagnostic Criteria of diabetes mellitus.

Without regard to time since the last meal, blood glucose concentration $\geq$11.1(mmol/L)/200mg/dl, with symptoms of diabetes

(or)

plasma glucose $\geq$7.00mmol/L (126 mg/dl) after a fasting for atleast 8 hours

(or)

In the Laboratory certified according to AIC standards, AIC >6.5%

(or)

Two hours post 75g glucose load plasma glucose >11.1 mmol/L (200mg/dl).

These criteria should be confirmed once again on different day if there is no unequivocal hyperglycemia and acute metabolic decompensation.

Diagnostic Criteria of DKA:

Diabetic ketoacidosis consists of biochemical triad of hyperglycemia, ketonemia and acidemia. Each of these features by itself can be caused by other metabolic conditions. Diagnosis of ketoacidosis is based on the characteristic clinical features and biochemical abnormality. The differential diagnosis includes hyper osmolar hyper glycemic non ketotic coma.

Laboratory Parameters:

Hyper glycemia $\geq$250 mg/dl

Acidosis (PH-6.8-7.3) and/or serum HCO3 <15meq/L

Ketonuria or Ketonemia

Pathogenesis:

DKA is a medical emergency that is due to relative or absolute insulin deficiency along with excess of glucagon, catecholamines, cortisol and growth hormone. (1, 3, 4, 8-13).

In DKA, there is increased hepatic gluconeogenesis and renal glucose output combined with decreased glucose uptake in peripheral tissues due to insulin deficiency lead to hyperglycemia inturn leads to increased osmolality of extracellular fluid, (1, 3, 10-17).

In type 1 diabetes mellitus there is total or relative absence of insulin leads to pure DKA not associated with significant hyper osmolarity.

The development of DKA needs both insulin deficiency and glucagon excess.

The insulin deficiency and counter regulatory hormones in excess lead to increased lipolysis and release of fatty acids from adipose tissues.

The free fatty acids are converted to beta hydroxy butyrate and acetoacetate by liver resulting in ketosis and metabolic acidosis (18).

The excessive glucose in blood leads to osmotic diuresis so loss of water, sodium, potassium and other electrolytes occur in DKA (6, 15-17).

Reactive oxygen species are produced during DKA, as DKA is one of the pro inflammatory state lead to oxidative stress.

The levels of lipid peroxidation markers, pro inflammatory cytokines, plaminogen activator inhibitor type 1 and C-reactive protein (CRP)

all are elevated in diabetic ketoacidosis, returns to normal once insulin therapy is started and hyper glycemia is controlled (19).

PRECIPITATING FACTORS:

The Most common precipitating factor is omission of insulin particularly in type-1 diabetes mellitus in young adults, (1, 4, 8-12).

Infection is also one of the most common precipitating factors causing DKA (1, 4, 8-12).

Other Causes:

Acute Pancreatitis.

Acute myocardial infarction.

Acute cerebrovascular accident

Drugs that affect glucose metabolism like glucocorticoids, thiazides, dobutamine, terbutaline (10), Anti Psychotics particularly second generation lead to development of DKA (20).

Omission of insulin in type 1 diabetes, and new onset type 1 diabetes may present themselves as DKA.

In children, adolescents and adults with type-2 DM, cases have been reported without identifiable precipitating factors.

In those cases, high rate of obesity, strong family history of diabetes, measurable pancreatic reserve, less prevalence of auto immune markers of B cell destruction, and ability to discontinue insulin therapy during follow up, are the important clinical and metabolic features (28, 29).

So this kind of type-2 diabetes is otherwise called with various names like type 1.5 diabetes, flat bush diabetes, idiopathic type-1 diabetes, atypical diabetes, and type 2 diabetes-ketosis prone (24, 30).

Those cases have severe deficiency of insulin secretion and their action, in early stage (25, 26, 29), but when they are treated with insulin aggressively, they become normal in due course, showing improved beta cell function after a few months of follow up (25, 27).

Around 40% of patients with type-2 DM (ketosis prone), remains as non-insulin dependent even after 10 years of achieving near normoglycemic remission showing greater recovery of basal and stimulated insulin secretion (24-27).

DIAGNOSIS:

History and Physical Examination

In both type 1 and type 2 diabetes mellitus, the evolution of the acute DKA is shorter (≤24 hr).

The symptoms of poorly controlled diabetes like polyuria, poly dipsia etc. may be present for months, but the alterations in metabolic parameters typical of DKA develops in short period only. It is typically less than 24 hours.

Polyuria,

Polydipsia,

Weight loss

Vomiting

Abdominal Pain

Dehydration

Weakness

Mental status changes

Coma

These are the classic clinical features of patients with DKA.

Poor Skin turgor

Kussmaul respiration

Tachy cardia

Hypotension

Alteration in mental status,

Ultimately coma

These are other physical findings present in DKA.

These DKA patients may have coffee ground vomiting that is guaiac positive. Upto 25% patients can have emesis like this.

The spectrum of mental status changes are from full alertness, profound lethargy to coma.

The peripheral vasodilation leads to hypothermia. (32) They can be even normothermic.

The presence of hypothermia is one of the poor prognostic marker of DKA.

In 50-70% of DKA cases, abdominal pain may be main symptom mimicking an acute abdomen. (33, 34).

When the hyperglycemia and metabolic acidosis is corrected, the abdominal pain usually gets corrected.

Hemiparesis, hemianopsia and seizures (partial motor seizures more common than generalised) may be the presenting features in some cases. These usually resolve once metabolic parameters are corrected.

Laboratory Findings:

Hyper glycemia

Ketonemia

Metabolic acidosis

are the Bio chemical triad of DKA

Increased anion gap metabolic acidosis results from accumulation of ketoacids.

The sum of chloride and bicarbonate is subtracted from the sum of sodium [Na-(Cl-+HCo_3)] to calculate anion gap.

The normal anion gap calculated in <12$\pm$2meq/L.

So the diagnosis of increased anion gap metabolic acidosis needs a anion gap of $\geq$10-12meq/L.

The severity of metabolic acidosis (blood ph, bicarbonate, ketones) and the presence of altered mental status are factors considered to classify the DKA into mild, moderate and severe (1).

According to the blood ketone concentration there will be leukocytosis in patients with hyper glycemic emergencies (2, 10). In the presence of hyperglycemia, there will be shift of water from intracellular space to extracellular space, so the extracellular sodium on admission will be low.

But the profound water loss can lead to increased extra cellular sodium, so increased extracelluar fluid sodium may indicate profound dehydration.

If the plasma is not cleared of chylomicrons, Pseudo hyponatremia and pseudo normoglycemia can occur in hyperglycemic emergencies (37, 38).

Due to an extracellular shift of potassium caused by insulin deficiency, acidemia and hypertonicity and the serum potassium concentration can get elevated (3, 10, 39).

The treatment with insulin lowers the potassium, so in patients with low serum potassium concentration the insulin therapy can provoke

cardiac dysrhythmia. So these patients require intense cardiac monitoring, and they should be given potassium replacement adequately.

There is positive linear relationship between mental status change and serum osmolality, which is proven by studies on mental alteration and serum osmolality (14).

The presence of other causes of mental status changes should be considered, when patient presents with stupor or coma, but with no definite rise in serum osmolality (320 mosm/kg).

After the assessment of clinical features and laboratory features DKA can be classified into mild, moderate and severe types.

VARIABLES	MILD	MODERATE	SEVERE
Blood glucose mg/dl	>250	>250	>250
PH	7.25-7.3	7-7.24	<7
HCo_3^-	15-18	10-<15	<10
Serum Ketone	+ve	+ve	+ve
Urine Ketone	+ve	+ve	+ve
Osmolality	Variable	Variable	Variable

Anion Gap	>10	>12	>12
Mental Status	Alert	Drowsy	Stupor or coma

Differential Diagnosis

The clinical history and the plasma glucose concentrations that range from little elevated (rarely >200mg/dl) to even below normal, distinguishes the starvation ketoacidosis, alcoholic ketocidosis from diabetic ketoacidosis. So all patients with ketoacidosis may not be having DKA.

In starvation ketosis, the serum Bicarbonate concentration is not reduced to less than 18 meq/L usually, but in alcoholic ketoacidosis it is reduced.It can result in very severe metabolic acidosis.

High anion gap metabolic acidosis producing conditions like lactic acidosis, ingestion of drugs like salicylates, ethylene glycol, paraldehyde, methanol and chronic renal failure should be differentiated from DKA.

DKA can be presenting manifestation of undiagnosed acromegaly. There are case reports showing this. (45, 48).

Treatment of Diabetic Ketoacidosis:

Intra venous fluid replacement and Insulin therapy are the cornerstones in the treatment of DKA. After these, the precipitating factor should be identified as early as possible, and it should be treated promptly and aggressively.

A Ryle's tube insertion should be done in all patients with complaints of vomiting and altered mental status, to prevent the aspiration induced pneumonitis.

Careful monitoring and periodic reassessment to confirm, that the patient is getting well and metabolic derangements are improving, are needed and it is central to successful treatment of DKA.

Chronological changes in vital signs, fluid intake, output and laboratory values as a function of insulin administered should be recorded in a comprehensive flow sheet.

The first step in the management of DKA is to confirm the diagnosis by three laboratory parameters, plama glucose, positive serum ketones, metabolic acidosis. Then the patient must be admitted in hospital preferably in intensive-care setting if ph is less than 7, or if unconscious or if treatment monitoring is needed. Assessment of serum Na+, k+, mg2+, Cl, HCo3, Po4 and acid base status (ph, hco3, pco2, hydroxybutyrate), renal function (creatinine, urine output) should be done at frequent interval. The next step is replacement of fluids. 0.9% saline, 2-3 litres should be infused over 1-3 hours, followed by 250-500ml/hr infusion of 0.45% saline followed by 150-250ml/hr infusion of 0.45% saline along with 5% glucose when the plasma glucose reaches concentration of 200mg/dl.

Next step in the management is, administration of short acting insulin that is 0.1 units/kg stat iv dose followed by 0.1 units/kg/hr iv infusion.

If there is no reponse by 2-4 hrs infusion rate can be increased to two or three fold.

Insulin therapy is not given when the initial plasma potassium is less than 3.3 meq/L. It can be started once the potassium is corrected. There is no supplementation of potassium is needed if the initial potassium is >5.2meq/L. until the potassium is corrected. Next step is the workup for precipitating factor, that is blood cultures, chest x ray, ECG to find what precipitated the event (non compliance, infection, trauma, infarction, cocaine).

Measurement of serum electrolytes (K+, HCO-3, Phosphate) and anion gap every 4 hours and measurement of capillary blood glucose every 1-2 hr is mandatory in the management of DKA.

Blood pressure, pluse, respirations, mental status changes, fluid intake and urine output should be monitored every 1-4 hrly.

When the ECG is normal, urine flow and creatinine are documented normal, potassium can be replaced. Potassium 10meq/hr can be infused if the serum K+ value is less than 5.2 meq/L. It can be increased upto 40-80meq/hr when the serum k+ is less than 3.5meq/L. or if bicarbonate is given.

The goal is to achieve the concentration of glucose 150-250mg/dl. Until this, management should be continued then the insulin infusion may be decreased to 0.05-0.1 units/kg/per hour.

Once the patient started to eat, long acting insulin can be started. It is better to allow the overlap of insulin infusion and subcutaneous insulin injection.

Complications:

1. Hypokalemia and hypoglycemia because of insulin overdosage, are the most common complications.

2. 0.7-1.0% of children with DKA manifest themselves with cerebral edema frequently fatal but rare complication. It is common in newly diagnosed diabetes, particularly in children. The clinical features of cerebral edema are deterioration in the level of consciousness, decreased arousal, lethargy, headache, seizures maybe the presenting manifestations. The deterioration of neurological status is rapid. Incontinence, respiratory arrest, pupillary changes can accompany. These symptoms increases when the herniation of brain stem occurs.
3. Hypoxemia
4. Non cardiogenic pulmonary edema.

Both these can complicate the treatment of DKA.

Hypoxemia occurs due to the increased lung water content and decreased lung compliance attributed to the reduction in colloid osmotic pressure (10).

Patients with DKA who is having crepitations on respiratory system auscultation and increased alveolo arteriolar oxygen gradient noted on initial blood gas measurement seem to be high risk for the development of pulmonary edema.

5. Hyper chloremia
6. ARDS
7. Acute gastric dilatation
8. Thrombo embolism
9. Hyperglycemia
10. Fluid overload

Long term Management:

Once the hyperglycemia is controlled, blood ketone reading is less than 1.0mmol/L, patient is eating well, and clinically stable, then the patient should be switched over to subcutaneous insulin therapy.

One hour after the first dose of subcutaneous insulin, intravenous infusion of insulin can be stopped.

Then the patient can be referred to specialized team of diabetologists for the further management.

How to prevent DKA:

In newly diagnosed type 1 diabetes, education should be focused on raising the awareness of symptoms of hyperglycemia and also hypoglycemia in order to prevent DKA.

The metabolic derangements should be diagnosed earlier and prompty intervened to prevent the DKA in already established type 1 DM.

The development of glucose levels (>15mmol/L), may create a dilemma for patients and health care givers managing type 1 diabetes, because

of risk of developing DKA, even though the home monitoring of blood glucose is well established.

Patients can reduce the unnecessary hospital visits and more invasive tests by utilizing the point of contact testing facility by patients themselves and health care professionals.

Beta hydroxy butyrate will not raise more than 1mmol/litre in patients with type 1 diabetes, who do not have metabolic derangement.

Better access to medical care, good communication with health care giver during episodes, and proper education can prevent many cases of DKA and HHS. Stoppage of insulin because of poor economic condition of family is one of the major cause of DKA in developing countries, insists the need of health care delivery system to look after this problem. Patient should be taught or how to manage themselves during illness, that is when to contact health care giver, ways to suppress infection and fever, use of supplemental rapid acting

insulin during illness and glucose goals and taking easily digestible liquid diet mainly of carbohydrate and salts. Patients should be advised to never discontinue insulin therapy. Family members should be taught how to measure blood glucose, monitoring of pulse, respiration, temperature, urine output and body weight.

Serum Amylase

It is a heterogeneous calcium dependent metallo enzyme of M54-62kDa. There are 2 iso enzymes exist: P type – Pancreatic, S-type-non Pancreatic. Highest activities of P-type enzyme is found in exocrine pancreas. S-type enzymes highest activities is being found in salivary glands. It has a very wide tissue distribution. Pancreatic acinar cells synthesize P-type amylase and secreted into the intestinal tract through the ductal system of pancreas. The mild alkaline condition of duodenum favours the action of P-type amylase.

The S-type amylase is synthesized in salivary glands, and it starts the hydrolysis of starch when the food is swallowed and passing through the

mouth and esophagus. The acid in the stomach terminates the action of S-type amylase.

Extracts of testes, ovaries, fallopian tubes, mullerian ducts, striated muscle, lungs, adipose tissue, semen, colostrum, tears and milk are some of organs and secretions, where S-type amylase can be found.

Kidneys excrete about 25% of plasma amylase, but the majority of excreted amylase is reabsorbed by the proximal tubules

Macroamylasemia may complicate the measurement of serum amylase level. In macroamylasemia, the macro molecular complex that is made up of immunoglobulin and enzyme is very large to be excreted by the kidneys. So the values may be falsely high. It leads to misdiagnosis of some abdominal conditions and erroneous treatment.

In acute pancreatitis some times serum amylase levels maybe normal because of the associated hyperlipedemia in this condition, for the reasons not known.

Hyper amylasemia causes:

1. Pancreatitis, Pancreatic trauma, pancreatic tumors etc, are some of the pancreatic diseases showing elevated P-type amylase.
2. Intra abdominal diseases: (eg) biliary treat diseases, obstruction, mesenteric infarction, liver disease, acute appendicitis – showing elevated P-type amylase
3. Salivary gland infection, trauma, irradiation can cause raised S-type amylase.
4. Tumoure of ovaries, prostate, testes, esophagus, thymus, thyroid, lung, ruptured ectopic pregnancy, and renal diseases including renal insufficiency can cause raised S-type amylase.
5. HIV, DKA, macroamylasemia and various drugs (opiates, diuretics, steroids) are miscellaneous conditions causing elevation of serum amylase.

SERUM LIPASE

The triglycerides are hydrolysed by lipase. There are many forms of lipase available

1. Pancreatic lipase
2. Colipase
3. Lipoprotein lipase

When there is decreased renal function, there will be elevated levels of coliapse, because coliapse is excreted by kidney. Lipoprotein lipase is essential in triglyceride hydrolysis, it is synthesized by vascular endothelium.

CAUSES OF INCREASED LIPASE:

Drugs: lipase values are increased by corticosteroids.

Acute pancreatitis: When pancreatic acinar tissue is destroyed, the pancreatic enzymes are released in to the pancreas and peritoneal cavity.

Gastrointestinal disease: lipase values are 2-3 times increased by peritonitis, bowel obstruction, visceral obstruction (laparotomy). Neoplasia and hepatic diseases.

Decreased renal function: Decreased renal function can increase the lipase values upto 4 times the normal. When the lipase values are more than 3-4 times, diagnosis of pancreatitis should be considered, even if the patient is azotemic (5).

There are studies reporting non specific hyper lipasemia in patients with DKA. Only few possible explanations can be offered to this finding. The molecular weight of lipase is 46-52KD is filtered in the kidneys to get reabsorbed by the renal tubules. In renal tubules the lipase gets metabolized. In DKA patients even with normal renal function the handling of lipase by the kidneys is compromised due to hypovolemia. So it may cause the elevation of serum lipase.

When pancreatic beta cells are destroyed by immune mediated attack in type I DM, spillover causes the pancreatic acini to get damaged ,thereby causing elevated serum lipase levels due to release in to the serum.

Diabetic ketoacidosis – hyper amylasamia and hyperlipasemia:

In 16-25% of the time in DKA, increased amylase and lipase occurs (49) without actual pancreatic involvement. DKA can be precipitated by acute pancreatitis. Acute pancreatitis can present or co exist or aggravate its severity. (50) In DKA, there have been reports of elevated serum amylase (51).

7 Out 13 Patients with DKA had elevated concentrations of serum amylase found in one study (51).

Polyacrylamide gel electrophoresis prooved that 6 out 7 cases where salivary gland amylase not pancreatic amylase. So there is proof available that pancreas is not the source of elevated amylase usually. Systemic

derangement of carbohydrate metabolism in DKA can cause hyper amylasemia since salivary type amylase are widely distributed in glandular epithelium. The stomach and intestinal epithelium can release lipolytic enzymes in to the circulation in the presence DKA. When GFR is reduced due to the dehydration in DKA, it can lead to elevated serum lipase levels, without actual pancreatic involvement.

Hyper amylasemia has been reported very frequently in patients with DKA. Abdominal tenderness, vomiting, pain present in more than 50% of patients with DKA. Previously this findings were attributed to the diagnosis of acute pancreatitis. But recent studies proved that acute pancreatitis is rarely present in DKA, so that the abdominal symptoms and hyper amylasemia cannot be attributed to the presence of acute pancreatitis.

During episodes of DKA, hyper amylasemia develops during hospitalization, not in the initial phase of DKA.

The range of elevation of amylase level is variable in DKA. It ranges from mild elevation to six times the normal limit which is usually considered

specific for acute pancreatitis. But in DKA, the abdominal symptoms and hyperamylasemia has no correlation between them. The hyperamylasemia is present in both groups of patients with abdominal symptoms and without abdominal symptoms in equal frequency.

In majority of patients with DKA and hyper amylasemia it is proven that the elevated amylase is mainly salivary type of iso amylase not pancreatic iso amylase. Salivary iso amylase includes all forms of iso amylase except pancreatic iso amylase, so exact source of origin of iso amylase is not known.

Metabolic acidosis may cause elevated serum amylase. Studies showing that metabolic acidosis or respiratory acidosis in the absence of DKA or renal failure can cause elevated amylase levels. (56) But this relationship with metabolic acidosis and hyper amylasemia is not statistically significant. Some other studies showing the results of elevated serum amylase is salivary iso amylase from unknown source.

DKA and Acute Pancreatitis

There are two important associations between DKA and acute pancreatitis should be recognized

1) In type II diabetes mellitus, there is increased incidence of gallstone formation because of obesity, so here acute pancreatitis can be triggered after the passage of gall stones.
2) Type V hyperlipoproteinemia is associated with high risk for acute pancreatitis. In DM the patients usually have type IV hyper lipoproteinemia, in susceptible patients it can turn in to type IV hyper lipoproteinamia with increased fat intake.

MATERIALS AND METHODS

SETTING

The study was conducted in the inpatients admitted in the Rajiv Gandhi Government general hospital Chennai

STUDY DESIGN

Single Center

Cross Sectional Study

STUDY PERIOD

Study was conducted between may 2012 and October 2012 for a period of 6 months.

SAMPLE SIZE

In the study period of 6 months, among the patients admitted in internal medicine ward after applying inclusion and exclusion criteria, 50 patients were included in this study.

The patients who fulfilled the criteria for DKA were taken in to the study.

Criteria for Diabetic keto acidosis:

1. Hyper Glycemia ≥ 250 mg/dl
2. Metabolic acidosis (Ph 6.3-7.3) and/or serum bicarbonate < 15 meq/L
3. Ketonuria or ketonemia

Inclusion Criteria

1. Age: >18yrs
2. Sex: Either Sex

3. DKA of any cause, both type I and type 2 DM

Exclusion Criteria

1. Patients with renal failure
2. Chronic Alcoholics
3. Patients with chronic Pancreatitis
4. Patients with Pancreatic trauma
5. Patients with Pancreatic tumours
6. Patients with intestinal obstruction
7. Patients with cholecystitis
8. Patients with bowel perforation

Detailed clinical history was taken from all the patients who were included in the study. History of Symptoms of DKa and acute pancreatitis like polyuria, polydipsia, breathlessness, abdominal pain, abdominal distention,

nausea, vomiting, loose stool, fever, dysuria, myalgia, chest pain, mental disturbance were elicited.

The past history including whether the patient was having type 1 or type 2 diabetes mellitus, precipitation factors like omission of insulin elicited. Past history of hypertension, hyper lipidemia, jaundice, TB, epilepsy, CAD, CKD, CVA, thyroid abnormalities, were analyzed. Drug history, personal and family history all were elicited.

After taking the detailed history, all the patients were examined clinically in detail. A detailed general examination was done including, nourishment, pallor, fever, mental status changes, icterus, clubbing, pedal edema, significant lymphadenopathy, cyanosis.

Vital signs like pulse, blood pressure, temperature, respiratory rate were taken. All the systems were examined carefully including optic fundus.

The following investigations were performed

1) Compete blood count – to find the anemia, leukocytosis, infections.
2) Renal function tests- urea, creatinine, sodium, potassium, blood glucose.
3) Liver function test – total bilirubin, Direct bilirubin, Alkaline phosphatase, transaminases, total protein, albumin, globulin.
4) Chest Xray
5) Electro cardiogram
6) Urine routine- Albumin, sugar, deposits
7) Urine acetone
8) Serum calcium, phosphorous, magnesium, chloride
9) Arterial ph
10) $P_a Co_2$
11) Serum bicarbonate
12) Urine culture & Sensitivity
13) Serum osmolality calculation
14) Serum lipid profile –Total cholesterol, Triglycerides etc.
15) Serum Amylase and lipase estimation

The normal values are

Serum amylase 20-96 U/L

Serum lipase 3-43 U/L

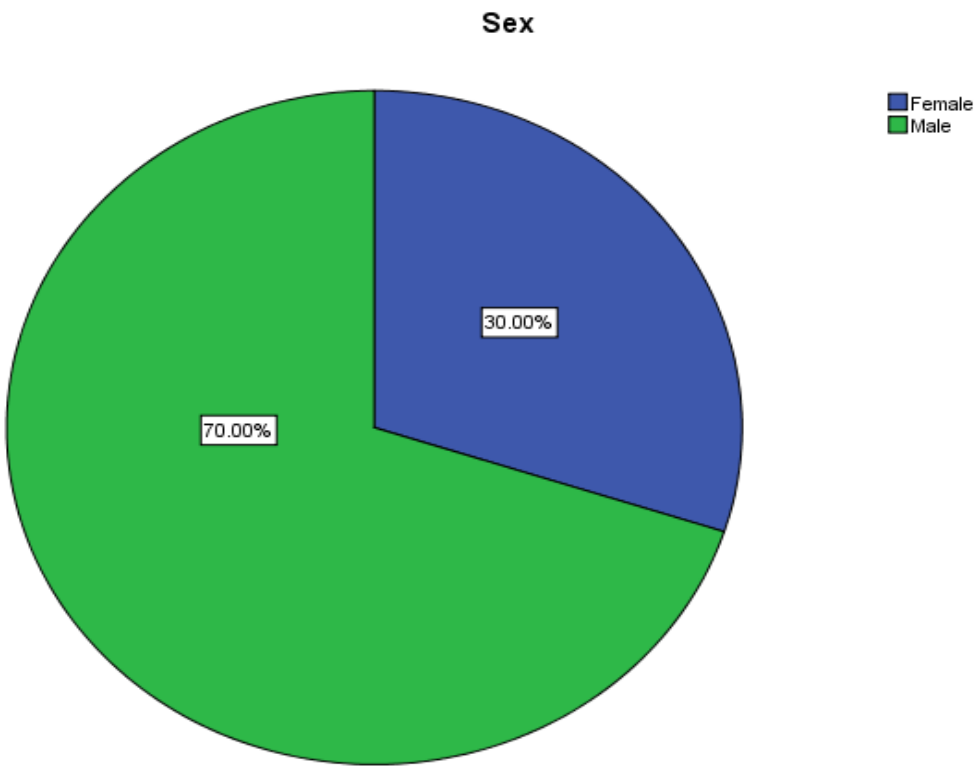
In patients with DKA who shows the elevation of serum amylase and/or lipase, were done following imaging modalities to diagnose acute pancreatitis

16) USG abdomen

17) CECT abdomen.

RESULTS AND OBSERVATIONS

Among the 50 patients included in our study, 35 patients were males accounting for 70% of the total cases. The remaining 30% of the patients, that is 15 cases were females.



Distribution of sex in the study- figure-1.

Among the 50 cases of DKA, 10 cases (20%) belong to type-I DM.

The remaining 40 cases (80%) belong to type II DM.

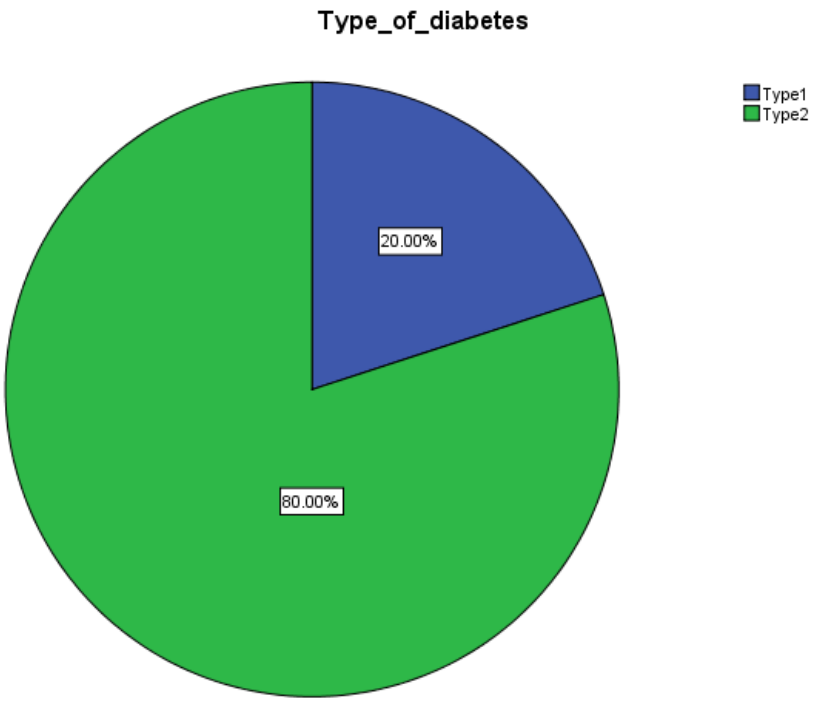


Figure-2 Distribution of type of DM in the study.

Among the 50 cases of DKA in our study, the precipitating factors that led to DKA were assessed.

1. Omission of insulin-9 cases-(18%)

2.CVA-13 cases (26%)

3. Acute MI- 8 cases (16%)

4. Infection- 11 cases (22%)

5. No identitable cause- 9 cases (18%)

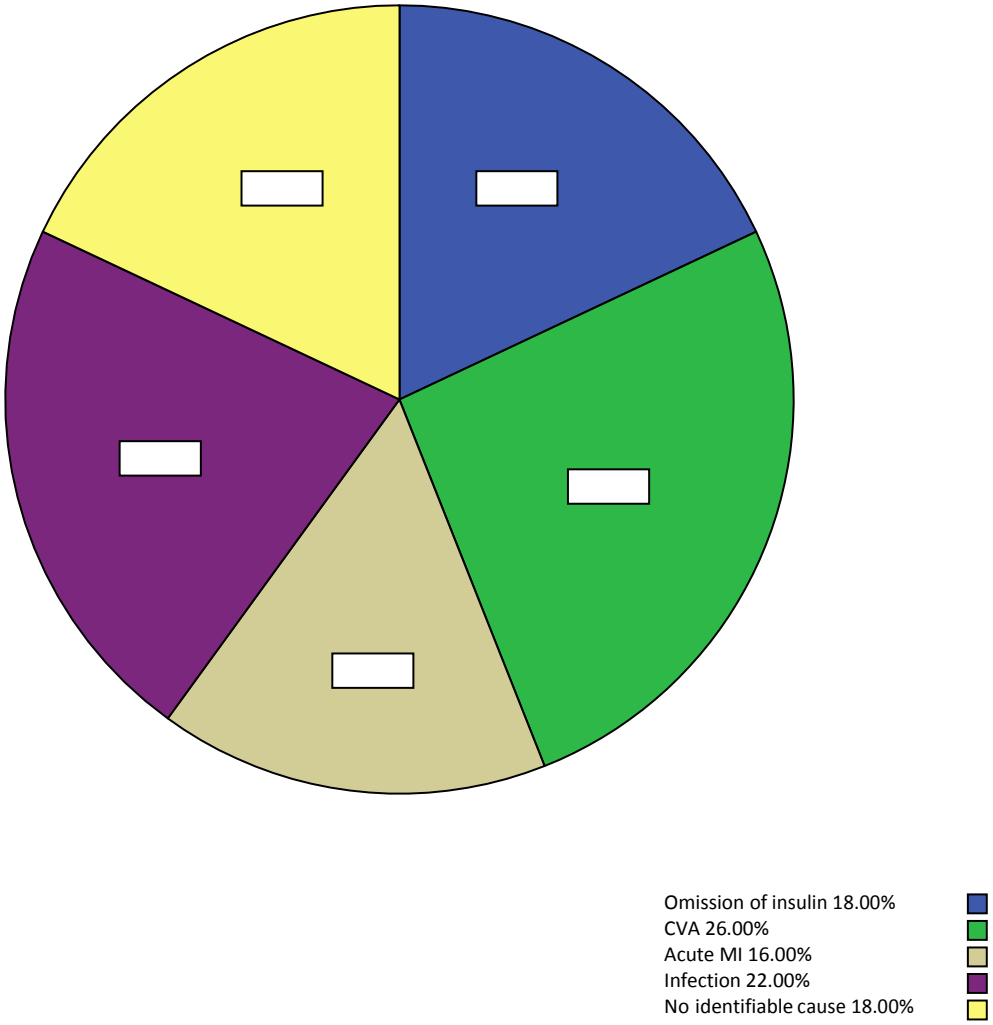


Figure-3. Distribution of precipitating causes of DKA in the study.

Among the 50 patients of DKA studied, 7 cases showed (14%) elevated serum amylase concentration.

Then elevated serum amylase levels were divided into 2 groups. One group has less than 3 times amylase elevation- in this group we had 3 cases (6%)

Next group has more than or equal to 3 times (≥3 times) amylase concentration elevation. In this group we had 4 cases-(8%)

No of cases with elevated serum amylase concentration -7 (14%).

Among these 7 cases

1) <3times elevation – 3cases (6%).

2) ≥3times elevation – 4 cases (8%)

Among the 50 patients of DKA studied, 14% of patients are showing elevation of serum amylase concentration.

But in those 14% cases were done USG abdomen and CECT abdomen to look for the evidences of acute pancreatitis.

None of the cases showed any evidence of acute pancreatitis, even in cases with more than 3times elevation of serum amylase concentration, that is usually considered specific for acute pancreatitis

No of cases with raised serum amylase concentration – 7(14%)

No of cases which showed evidences of acute pancreatitis among this group - 0

Among the 50 patients of DKA studied, 11 cases (22%) showed elevated serum lipase concentration.

Then these cases were grouped into two. First group has Less than 3 times elevation of serum lipase concentration. In this group we had 7 cases (14%).

Second group has patients with more than or equal to 3times (≥3times) elevation of serum lipase concentration. In this group we had 4 cases (8%).

No of cases with elevated serum lipase concentration-11 (22%)

Among these 11 cases

1) <3 times elevation – 7 cases (14%)

2)≥3times elevation – 4 cases (8%)

No of cases which showed any evidences of acute pancreatitis in the groups - 0

All the cases who showed elevated serum lipase concentration were done USG abdomen and CECT abdomen

But none of them showed any evidences of Acute pancreatitis even in cases which showed more than 3 times elevation which is usually considered more specific for the diagnosis of acute pancreatitis.

Finally it is concluded that

1. No of cases with non specific elevation of serum amylase in DKA-7 (14%).

2.No of cases with non specific elevation of serum lipase concentration in DKA – 11(22%).

Among the 50 patients of DKA studied 2 cases were died. Those cases were having serum concentrations of amylase and lipase in normal range only. So there is no evidence for the increased mortality in patients with elevated serum amylase and lipase.

No of cases studied-50

No of cases died-2(4%)

Normal serum concentration of amylase and lipase were present in those 2 cases.

Among the 50 patients of DKA studied, there were 3kinds of results

1. Normal

2. Elevation of lipase concentration exclusively

3. Elevation of both serum amylase and lipase concentration.

The distribution of these results among various variables like Na^+, K^+, Hco_3, urea, glucose, Type of DM, PH, osmolality were studied and any correlation between them were analysed. The results are following.

1. TYPE OF DIABETES MELLITUS:

No of cases				
Type of diabetes	Normal range	Lipase elevated	Both Amylase + lipase elevated	Total
1. Type I	7	2	1	10
2. Type II	32	2	6	40
Total	39	4	7	50

Table I – Distribution of amylase, lipase elevation among types of diabetes.

Out of 10 cases of type-I DM 7 cases were showing normal results. Only 3 cases were showing elevation of (30%) enzymes concentration. (2 cases – lipase only, 1 case both serum amylase + lipase elevated)

But in 40 cases of type2 DM, 32 cases were normal. 8 cases (20%) were showing abnormal results (2 cases- lipase only, 6 cases – both enzymes elevated).

Comparing these results, there is slightly increased number of cases were showing elevated serum concentration of amylase and lipase in type-I DM (30%) than type-2 DM (20%). But this is not statistically signifigant.

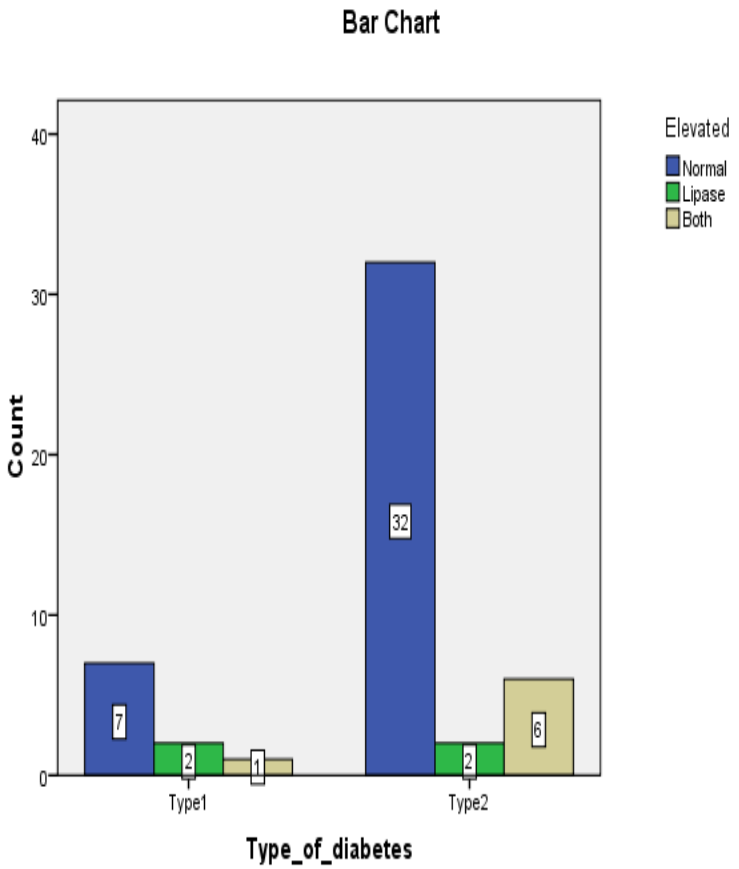


Figure-4 Distribution of serum amylase, lipase level among types of DM.

2. SERUM SODIUM

Serum Na^+ mmol/l.	No of cases			
	Normal	Lipase elevation	Amylase + lipase elevation	Total
1. <135	21	2	7	30
2. 135-145	13	2	0	15
3. >145	5	0	0	5
Total	39	4	7	50

Table-2 Distribution of serum amylase, lipase among various concentration of serum Na^+.

Among the 3 groups of serum Na^+ Concentration, the first group, that is with serum Na^+ concentration of <135mmol/L is showing more number of cases (30%) are showing combined elevation and exclusive lipase elevation than the 2nd group (135-145) which is showing 13.3% and 3rd (>145) group showing 0% only.

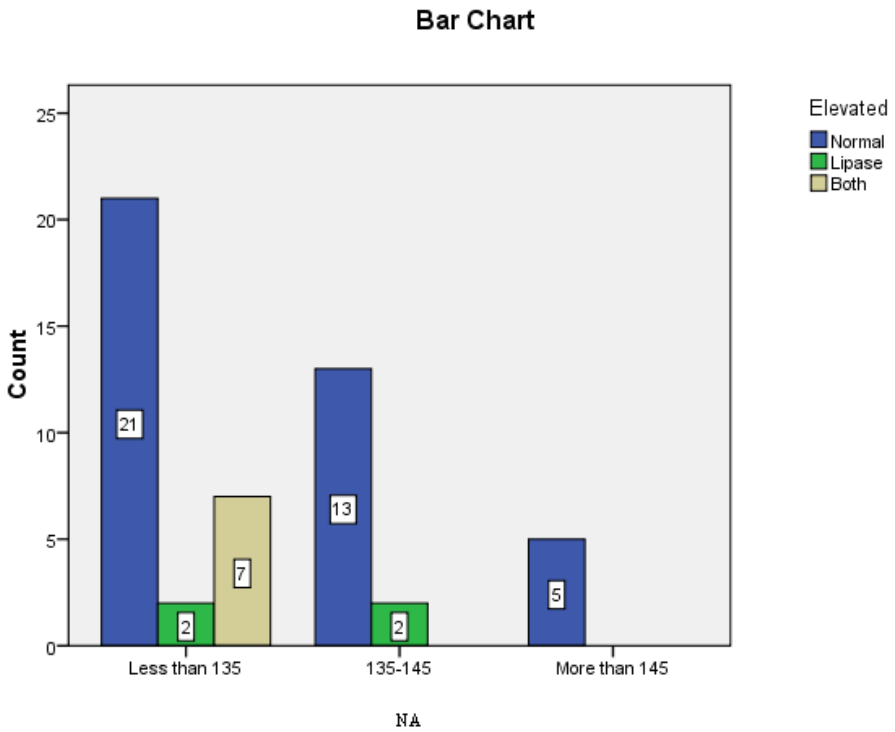


Figure -5 Distribution of serum amylase and lipase among various serum Na^+ concentrations.

3. SERUM POTASSIUM:

Serum k^+ mmol/l.	No of cases			
	Normal	Lipase elevated	Both Amylase + lipase elevated	Total
1) <3.5	0	0	1	1
2) 3.5-5	13	0	2	15
3) >5	26	4	4	34
Total	39	4	7	50

Table – 3 Distribution of serum amylase, lipase among, various concentrations of serum k^+

Among the three group of various k^+ concentration, only one case is distributed into concentration of <3.5 which is having elevation of both amylase & lipase (100%).

But in the second group (3.5-5 mmol/L) is showing 13% incidence of combined elevation and exclusive lipase elevation.

In the 3rd group (>5 mmol/L) 23% of cases are showing combined elevation and exclusive lipase elevation.

So amylase and lipase concentrations were high in patients with low K^+ and also high K^+ serum concentrations.

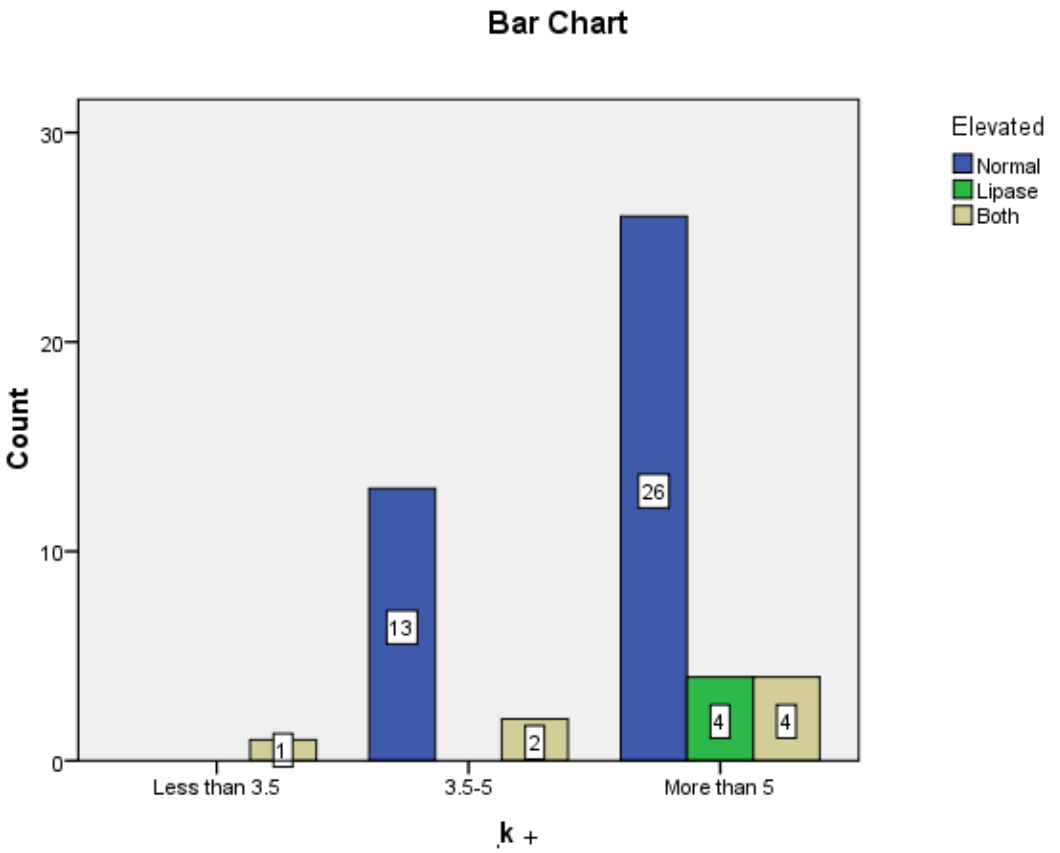


Figure-6- Distrubtion of serum amylase and lipase among various k^+ concentrations.

4. SERUM OSMOLALITY.

Serum osmolality mosm/kg	No of cases			
	Normal	Lipase	Combined elevation	Total
1. 275-295	9	0	1	10
2. >295	30	4	6	40
Total	39	4	7	50

Table-4 Distribution of serum amylase and lipase among different serum osmolality groups.)

Among the two groups studied, the first group (serum osmalility 275-295 mosm/kg) showed only 10% of cases have combined elevation and exclusive lipase elevation. But in the second group (>295 mosm/kg) 25% of cases showing combined elevation and exclusive lipase elevation.

So amylase and lipase concentrations were high in patients with increased osmolality

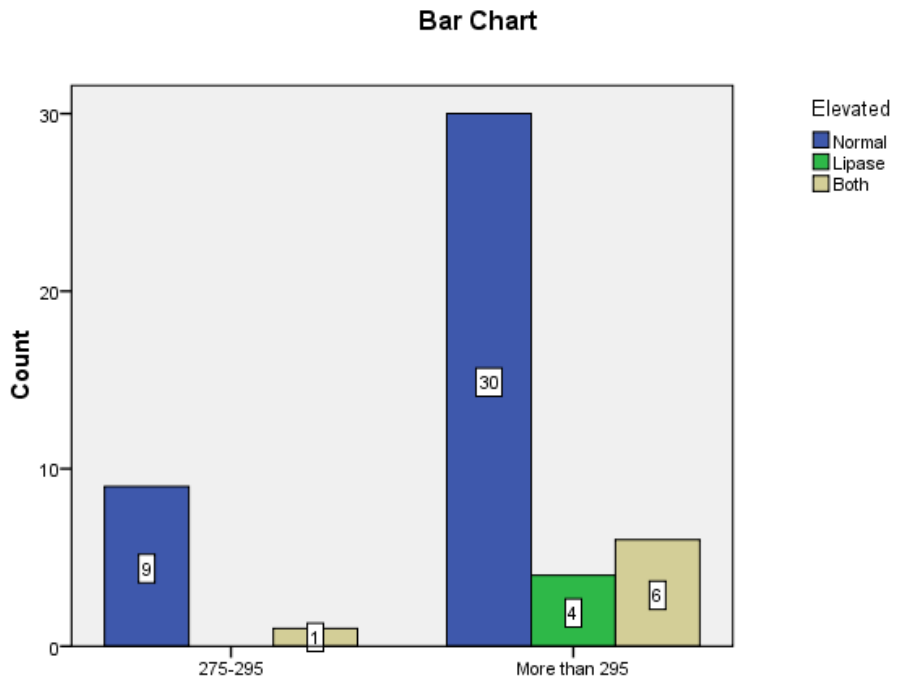


Figure-7

Distribution of serum amylase, lipase among different serum osmolality groups.

5. ARTERIAL PH.

Ph	No of cases			
	Normal	Lipase	Combined elevation	Total
1. <7	0	2	2	4
2. 7-7.24	30	2	4	36
3. 7.25-7.3	9	0	1	10
Total	39	4	7	50

Table-5 Distribution of serum amylase and lipase among different ph groups.

Among the different Arterial ph groups studied, there is all the cases (100%) in group (ph<7) showing combined elevation and exclusive lipase elevation.

But in the 2nd group (ph 7-7.20) only 16.6% of cases showing combined elevation and exclusive lipase elevation.

In the 3rd group (ph 7.25-7.3) only 10% of cases are showing combined elevation and exclusive lipase elevation.

So it can be concluded that fall in Ph is associated with elevated serum amylase and lipase concentration.

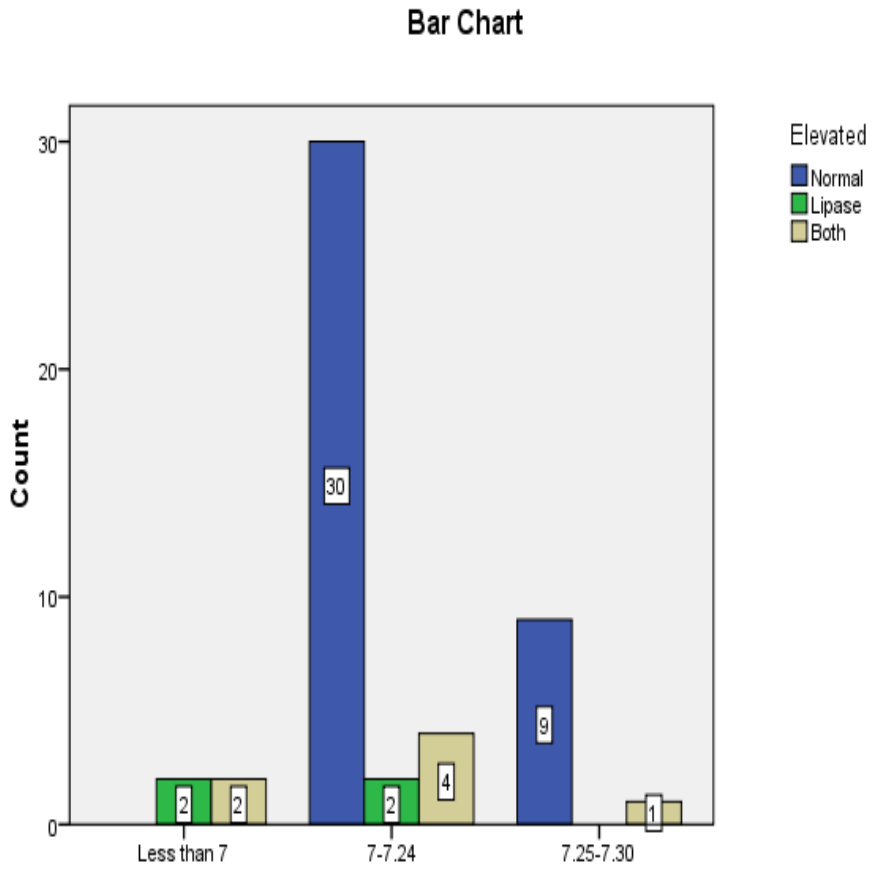


Figure-8 Distribution of serum amylase and lipase among various arterial ph groups.

6. SERUM HCO_3

Srum Hco_3 meq/L	No of cases			
	Normal	Lipase	Both	Total
1. Less than 10	1	1	1	3
2. 10-15	35	3	6	44
3. 15-18	3	0	0	3
Total	39	4	7	50

Table-6 Distribution of serum amylase and lipase among various serum Hco_3 groups.

Among the 3 groups of serum Hco_3 studied, the first group (serum Hco_3 <10) is showing that 66% of cases are having combined elevation and exclusive lipase elevation.

But in the second group (serum Hco_3 10-15) showing only 20% of cases are having combined elevation and exclusive lipase elevation.

In the 3rd group (serum Hco_3 15-18) no patients are having elevation of serum amylase and lipase concentration.

So it can be concluded that low bicarbonate values are associated with increased serum amylase and lipase concentration.

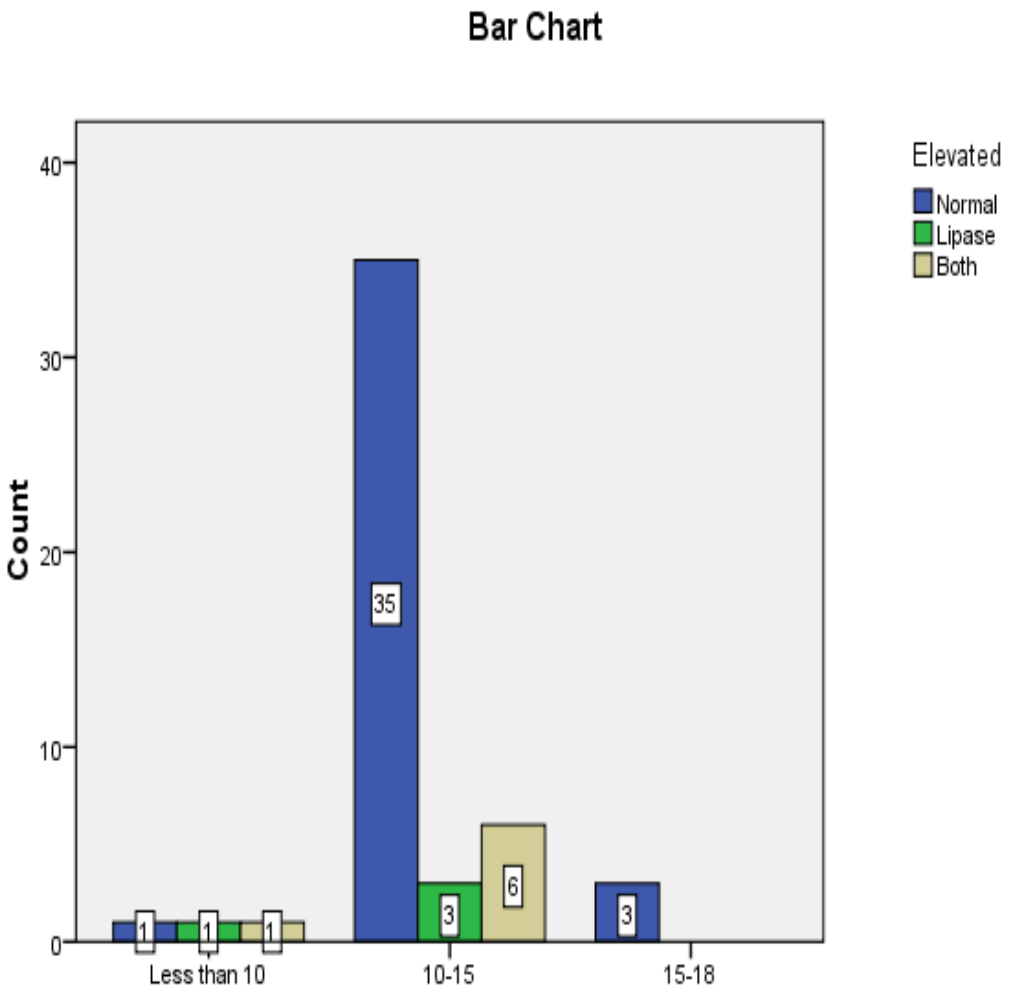


Figure-9 Distribution of serum amylase and lipase among different bicarbonate groups.

7. PLASMA GLUCOSE.

Blood glucose mgld1	No of cases			
	Normal	Lipase	Both	Total
1. lessthan 500	36	2	6	44
2. more than ≥500	3	2	1	6
Total	39	4	7	50

Table-7 Distribution of serum amylase and lipase among different blood glucose groups.

Among the two groups studied, there is increased incidence serum amylase and/or lipase concentration elevation in second group (blood glucose >,500mg/dl) that is 50% than the first group (18% only).

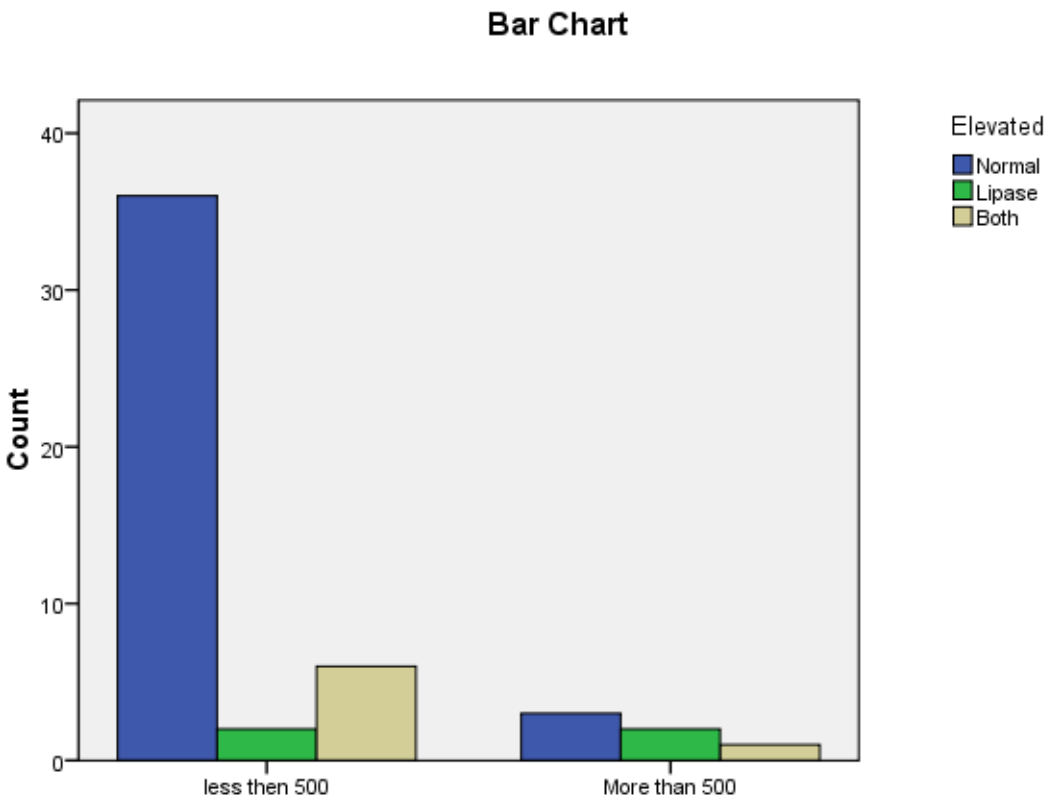


Figure-10 Distribution of serum amylase and/or lipase among different plasma glucose groups.

8. BLOOD UREA.

Blood urea mgldl	No of cases			
	Normal	Lipase	Both	Total
1. 40-60	20	2	1	23
2. 61-80	19	1	3	23
3. >80	0	1	3	4
Total	39	4	7	50

Table-8 Distribution of serum amylase and/or lipase among different blood urea groups

Among the 3 groups studied, there is increased (100%) serum amylase and/or lipase concentration elevation in patients with high blood urea (>80mg/dl) -3rd group than in the 2nd group (17.3%) and 1st group (13%).

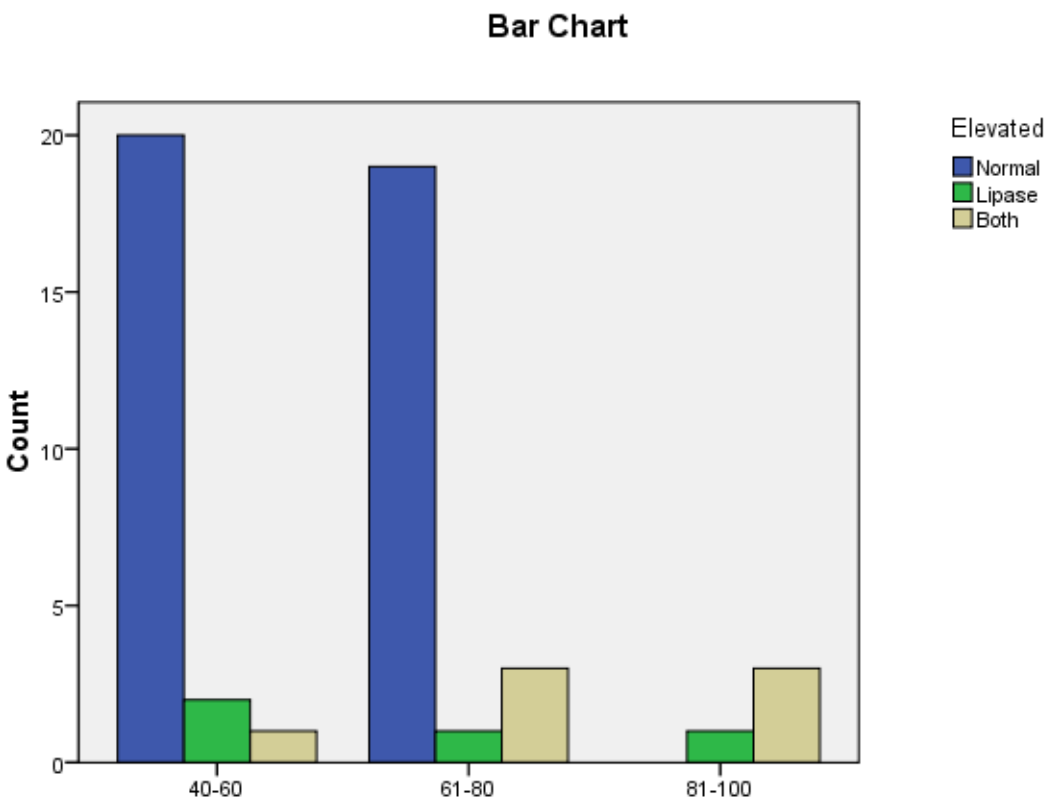


Figure-11 Distribution of serum amylase and/or lipase among different blood urea groups.

Mean value of serum amylase in patients with blood urea <60mgldl is 63.45. Mean value of serum amylase in patients with blood urea ≥ 60mg ldl is 115.56. Pvalue. 0.0518 Considered not quite significient

Mean value of serum lipase in patients with blood urea <60mgldl is 46.45. Mean value of serum lipase in patients with blood urea > 60mgldl is 52. The P. value is 0.65 This is statistically not significant.

Mean value of serum amylase in patients plasma glucose >500 mgldl is 94.3 mean value of serum amylase in patients with ≤ 500mg ld is 92.5. The P value is 0.96. statistically not significant.

Mean value of serum lipase in patients with plasma glucose >500 is 109.5. mean value of serum lipase in patients with plasma glucose ≤500 is 41.86. The P value is 0.0008 This is considered extremely significant.

DISCUSSION

Various authors have studied the serum amylase and lipase enzyme abnormalities in the patients of DKA. But most of the studies were unable to prove any relationship between the raise of serum amylase and lipase concentration and actual pancreatic involvement, probably of non specific elevation.

M.C. Vantyghem et al (52) measured serum total amylase (TA), pancreatic amylase (PA) lipase (L) and leukocyte elastase' in 4 groups of patients. 1st group consists of patients with DKA, 2nd group consists of patients with porly controlled non-ketotic DM. Third group patients are well controlled DM. Fourth group consists of Non DM persons.

The mean serum enzyme activities were significantly higher in group-1 than 2, 3, 4. In all the patients studied, the four enzymes have correlation between themselves and with glucose, BUN, HCO_3^- In group-1 the TA has negative correlation with serum HCO_3 and arterial Ph. Pancreatic amylase and lipase correlated with BUN and glucose positively and also it

had negative correlation with HCO_3 PA correlated with Ph positively. This study had a conclusion that raise of pancreatic enzymes correlated mainly with hyperglycemia, dehydration and acidosis

Vinicor F et al (53) concluded in his study that 79% of patients in DKA had hyper amylasemia with 48% are having pancreatic type amylase.

Fontaine P et al (54) concluded that the hyper amylasemia is subclinical and can represent the effects of hyper tonicity (or) hypo perfusion.

Kitabchi et al (55) in his study concluded that lipase is a more sensitive and specific indicator of pancreatitis but it can also get elevated in DKA

Eckfeldt et al (56) collected serum from 33 patients with metabolic or respiratory acidosis in the absence of diabetic acidosis or renal failure. The total serum amylase was elevated in 36% of these patients and five patients had marked elevations in a range usually considered diagnostic of acute pancreatitis.

Yadav D Nair et al (57) in their study, they evaluated 150 consecutive episodes of DKA in 135 patients. They were evaluated for serum amylase, lipase and biochemical markers of DKA on admission and 24 hours later.

Patients were divided into 3 groups according to the results, those were clearly non specific amylase elevation (<3 times), clearly non specific lipase elevation (<3 times). Probably non specific amylase or lipase elevation (>3 times). The results were, non specific amylase elevations in 16.6% of cases (10% if cases were showing more than 3 times elevation, and 6.6% if cases were showing less than 3 times elevation).

Non specific lipase elevation is present in 24% of cases, out of which 15.3% of cases were showing less than 3 times elevation and 8.7% of cases were showing more than 3 times elevation.

They have concluded that non specific elevation of amylase and lipase present in 16-25% of cases.

Amylase elevation is correlated with serum osmolality and ph, lipase elevation is correlated with serum osmolality alone.

Andrew L. Warshaw et al (58) found 7 out of 13 patients with DKA had raised concentration of serum amylase. Iso enzyme analysis confirmed that elevated amylase is salivary iso enzyme type not pancreatic type. They concluded that hyper amylasemia in DKA is most often due to carbohydrate metabolic derangements.

Nair's et al (59) observed 100 consecutive episodes of DKA during a period of 13 months. Careful history, CBC, ABG, Comprehensive metabolic assay, Serum amylase, lipase, and TG levels were estimated on admission and 48 hr later.

All patients with abdominal pain and elevated serum amylase and lipase levels were done CT abdomen to diagnose acute pancreatitis

They noted elevation of lipase in 29% and amylase in 21% of cases, without any CT evidence of acute pancreatitis

They concluded that elevation of serum lipase and amylase occur in DKA, but lipase levels elevation seems to be less specific than amylase level elevation for the acute pancreatitis diagnosis

A.H. knight et al (60) analyzed 35 consecutive episodes of DKA showed the elevated serum amylase concentration frequently.

In 60% of cases, there were elevation of amylase out of which 17% showed very high levels. They found that the initial blood sugar value of more than 500mg/dl and acute (<48hrs) onset of episode correlated with hyper amylasemia.

There were no evidences of acute pancreatitis in these cases, and no other causes of hyper amylasemia found. There is no increased mortality and morbidity associated with hyper amylasemia.

D.N. Williams et al (61) presented a case of diabetic with reduced GFR who developed lactic acidosis and hyper amylasemia after treated with

phenformin. There is no evidences of acute pancreatitis in that case. The patient succumbed.

So it is concluded that hyper amylasemia can be present in patients with lactic acidosis without any evidence of acute pancreatitis.

Ali A Rizvi et al (62) reported 2 cases of DKA with non specific elevation of serum amylase and lipase. He concluded that both amylase and lipase can get elevated non specifically in the setting of DKA without any significance. So both hyper amylasemia and hyper lipasemia are not diagnostive of AP in the setting of DKA.

In our study, we had 14% of cases were showing elevated serum amylase concentration, out of which 6% of cases were having less than 3 times elevation and 8% of cases were having more than 3 times elevation. But none of the cases showed any evidence of acute pancreatitis. This results are consistent with studies of M.C. vantyghem et al, Vincor F. et al, Yadav D. Nair et al, Andrew L. Warshaw et al, Nair S. et al, A.H. Knight et al, and Ali A. Rizvi et al.

In our study, we had 22% of cases were showing elevated serum lipase concentration. Out of which 14% of cases were having less than 3 times elevation and 8% of cases were having more than 3 times elevation. But no cases had any evidence of acute pancreatitis. All cases were having non specific elevation probably. This results are consistent with the studies of M.C. Vantyghem et al, kitabchi et al, Yadav D. Nair et al, Nairs et al, and Ali A. Rizvi et al.

Out study showed, that non specific lipase elevation present in more number of cases (22%) than non specific amylase elevation (14%). So lipase levels elevation seems to be less specific than amylase level elevation for the diagnosis of acute pancreatitis. This result is consistent with the results of Nair S. et al and Yadav D. Nair et al.

In our study, there is no increase in the mortality rate among the cases with elevation of serum amylase and/or lipase concentration. This is consistent with the studies of A.H. Knight et al.

In our study serum amylase and/or lipase concentration were elevated in those cases with high serum osmolality (>295 mosm/kg). This is consistent with studies of M.C. Vantyghem et al, Fontaine P. et al, Yadav D. Nair et al.

In our study, serum amylase and/or lipase concentration were elevated in those patients with arterial ph of less than 7. This is consistent with studies of M.C. Vantyghem et al, Eckfeldt et al, Yadav D. Nair et al, and D.N. Williams et al.

In our study serum amylase and/or lipase concentration were elevated in patients with serum bicarbonate of less than 10 meg/L. This is consistent with the results of M. C. Vantyghem et al.

In our study serum amylase and/or lipase concentration were elevated more in cases with high plasma glucose (>500 mg/dl). This is consistent with the studies of M. C. Vantyghem et al, and Andrew L. Warshaw et al.

In our study serum amylase and/or lipase concentration were elevated more in patients with high blood urea (>80mg/dl). This is consistent with studies of M. C. Vantyghem et al and D. N. Williams et al.

CONCLUSIONS

1. Elevation of serum amylase and lipase concentration occur in patients of DKA
2. 14% of cases with DKA are showing non specific elevation of serum amylase with no evidences of acute pancreatitis
3. 22% of cases with DKA are showing non specific elevation of serum lipase with no evidences of AP
4. Even more then 3times elevation of serum amylase and or lipase is not associated with AP
5. Among the precipitating causes of DKA, CVA leads, followed by infections, omission of insulin, myocardial infarction and no identifiable cause.
6. There is no increased mortality attributable to increased serum amylase and/or lipase concentration
7. There is increased serum amylase and/or lipase concentration in type I DM (30%) than type 2DM (20%)

8. There is increased serum amylase and/or lipase concentration in patients with decreased serum Na^+ concentration (<135 mmol/L).
9. There is increased serum amylase and/or lipase concentration in patients with both low k^+ (<3.5mmol/L) and high K^+ (>5mmol/L) concentrations.
10. There is increased serum amylase and/or lipase concentration in patients with high osmolality of serum (>295mosm/kg)
11. There is increased serum amylase and/or lipase concentration in patients with low arterial ph < 7
12. There is increased serum amylase and/or lipase concentration in patients with low serum bicarbonate (<10 meq/L)
13. There is increased serum amylase and/or lipase concentration in patients with high blood urea conentration (>80mg/d1)
14. There is increased serum amylase and/or lipase concentration in patients with high blood glucose (>500mg/dl) concentration.

15. Serum lipase concentration is elevated more in patients with plasma glucose of >500mg/dl, which is considered statistically extremely significant (p value0.0008)
16. There increased serum amylase and/or lipase concentration in patients with DKA in probably due to metabolic derangements not due to acute pancreatitis.

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ABBREVATIONS

DM – Diabetic Mellitus

DKA – Diabetic Keto Acidosis

AP – Acute Pancreatitis

TA – Total Amylase

PA – Pancreatic Amylase

SA – Salivary Amylase

L – Lipase

GFR – Glomerular Filtration Rate

PROFORMA

Elevated serum amylase and lipase levels without actual pancreatic involvement in the presence of diabetic ketoacidosis - an observational study

NAME:	**AGE/SEX:**
IP NO:	**WEIGHT:**
DOA:	**HEIGHT:**
COMPLAINTS:	**Yes/No**
Polyuria	
Polydipsia	
Breathlesness	
Abd-pain	
Abd. distension	
Vomiting	
Nausea	
Loose stool	

Fever

Dysuria

Myalgia

Others

Past H/o. DM - Type I/II Yes/No

Inadequate insulin (or) withdrawal of Administration

HT

Drugs

Jaundice

TB

Epilepsy

CAD

CKD

CVA

Hypo/Hyper Thyroid

Pancreatic Ca/ Tumour

Cholescystitis

Panereatitis

Personal H/O:

Alcoholic

Smoker

Family H/o.:

Occupational H/o:

Menstrual & Obst. H/o:

General Examination	**Yes/No**
Consciousness	
Orientation	
Pallor	
Icterus	
Clubbing	
Cyanosis	
Pedal Edema	
Lymph Node enlargement	

Dehydration - Mild/Moderate/Severe

Vital Signs:

PR

BP

RR

Temperature

JVP

Systemic Examination

CVS

RS

Abdomen

CNS

Investigations:

HB	gm/dl
Tc	cells/cu.mm
DC	P%L% E%
ESR	

Urea	mg/dl
Creatinine	mg/dl
Sugar	mg/dl
Na^{+}	meq/L
K^{+}	meq/L
Ca^{++}	meq/dl
PO_4^{3-}	meq/dl
Mg	
Cl^{-}	
Arterial pH	
$PaCO_2$	
Serum HCO_3	

Urine Examination:

Albumin

Sugar

Acetone

Deposits

Urine C&S

Liver Function Tests:

T.Protein

Albumin

Glubulin

Serum Lipid Profile:

Total Cholesterol

Triglyceride

12 lead ECG

Chest x-ray

USG abdomen

Serum Amylase

Serum Lipase

CT. Abdemen

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. C. Sangeshwaran
PG in MD General Medicine
Madras Medical College, Chennai -3

Dear Dr. C. Sangeshwaran

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Elevated serum amylase and lipase levels without actual pancreatic involvement in the presence of DKA " No.32042012.

The following members of Ethics Committee were present in the meeting held on 19.04.2012 conducted at Madras Medical College, Chennai -3.

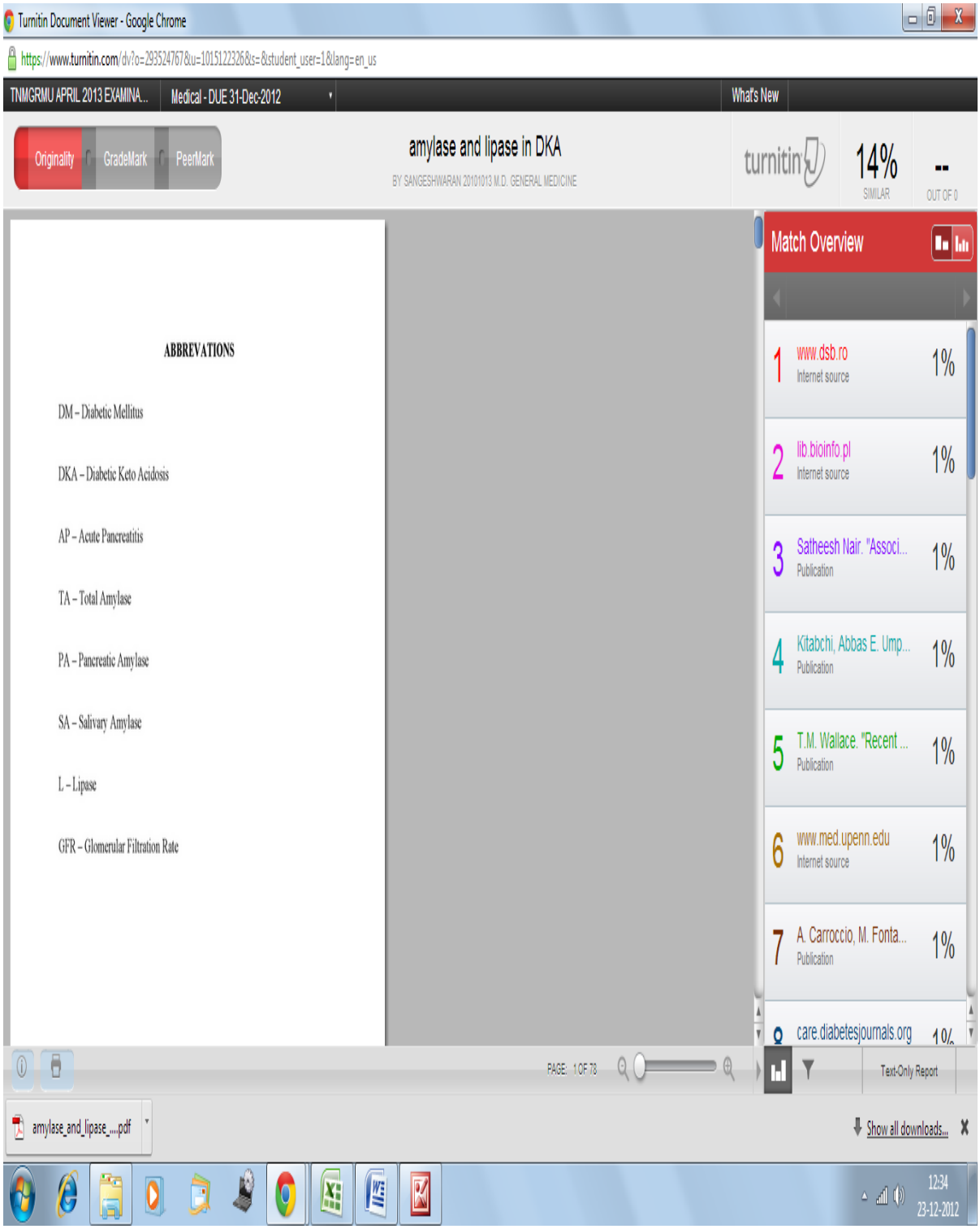
1.	Dr. S.K. Rajan. M.D.,FRCP.,DSc	-- Chairperson
2.	Prof. Pregna B. Dolia MD Director , Institute of Biochemistry, MMC, Ch-3	-- Member Secretary
3.	Prof. B. Kalaiselvi MD Prof. of Pharmacology ,MMC, Ch-3	-- Member
4.	Prof. C. Rajendiran, MD Director , Inst. of Internal Medicine, MMC, Ch-3	-- Member
5.	Prof. Md. Ali. MD.DM Prof & HOD, Dept. of MGE, MMC, Ch-3	-- Member
6.	Prof.P.Karkuzhali MD Director i/c, Prof., Inst. of Pathology, MMC, Ch-3	-- Member
7.	Prof. S. Deivanayagam MS Prof of Surgery, MMC, Ch-3	-- Member
8.	Prof. A. Radhakrishnan MD Prof of Internal Medicine, MMC, Ch-3	-- Member
9.	Thiru. S. Govindsamy. BABL	-- Lawyer
10.	Tmt. Arnold Soulina MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee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ABBREVATIONS
DM – Diabetic Mellitus
DKA – Diabetic Keto Acidosis
AP – Acute Pancreatitis
TA – Total Amylase
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L – Lipase
GFR – Glomerular Filtration Rate
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ABBREVATIONS DM – Diabetic Mellitus DKA – Diabetic Keto Acidosis AP – Acute Pancreatitis TA – Total Amylase PA – Pancreatic Amylase SA – Salivary Amylase L – Lipase GFR – Glomerular Filtration Rate INTRODUCTION Diabetes mellitus is a group of disorders characterized by chronic hyperglycemia associated with disturbances of carbohydrate, protein, and fat metabolism, due to absolute or relative deficiency in insulin secretion and /or action. Diabetes causes long term damage, dysfunction and failure of various organs especially the eyes, kidneys, nerves, heart and blood vessels. There are two types of diabetes mellitus present. Type-I DM - These patients depend on insulin for survival. There is...

S.No	Name	Age	Sex	IP.NO	Type of diabetes	Precipit factor	Urea	Creatinine	Sugar	Na	K	Serum osmalarity	PH	PaCO2	Serum HCO3	Amylase	Lipse
1	Maheswari	44	Female	42813	Type2	Omission	92	1.5	520	124	5.9	303	6.9	21	8	280	118
2	Saranya	20	Female	43257	Type1	No cause	58	1.2	512	134	6.1	328	6.9	28	11	52	252
3	Rajamanikam	60	Male	43590	Type2	SHT/CAD/NSTEMI	55	1.4	312	131	5.3	299	7.25	29	10	140	96
4	Karpagam	60	Female	45320	Type2	CAD/NSTEMI	59	1.1	389	136	5.4	314	7	32	14	80	128
5	Shanmugam	73	Male	48329	Type2	Inadequate insulin/CAD/NSTEMI	88	1.3	431	132	3.8	310	6.9	22	10	482	54
6	Stephan	19	Male	48374	Type2	Omission of insulin	72	1.2	412	124	3.1	289	7.1	21	12	104	150
7	Suresh nandha sharma	60	Male	50567	Type2	Omission	82	1.3	451	132	5.2	312	7.2	29	14	382	49
8	Appavoo	48	Male	50709	Type2	No cause	64	1.2	356	132	5.1	304	7.2	29	14	82	92
9	Vanjinathan	45	Male	50807	Type2	Omission	71	1.2	511	131	5.2	312	7.2	2.8	14	72	32
10	Girija	40	Female	52068	Type2	UTI	69	1.3	431	141	5.4	328	7.27	24	10	95	42
11	Shantha kumari	60	Female	52117	Type2	CVA	64	1.3	432	142	5.3	328	7.24	22	12	95	42
12	Periyasamy	18	Male	53139	Type2	New case	71	1.6	451	134	5.4	316	7.2	26	13	95	42
13	Perumal	70	Male	53219	Type1	CVA	56	1.2	451	126	3.9	294	7.25	29	13	95	42
14	Kumaresan	17	Male	53333	Type1	New case	54	1.4	512	138	5.2	323	7.25	25	15	95	42
15	kuppamma	45	Female	54598	Type2	Pneumonia	54	1.3	356	134	5.5	307	7.28	28	14	95	42
16	Jaya	56	Female	54729	Type2	Pneumonia	64	1.4	454	142	5.7	330	7.14	21	14	95	42
17	Kolanji	53	Male	55721	Type2	CVA	63	1.3	382	134	3.8	308	7.29	29	14	95	42
18	Moorthi	52	Male	55887	Type2	CVA	62	1.3	392	128	3.8	295	7.3	22	14	95	42
19	Badrakali	73	Female	59953	Type2	CVA	51	1.3	424	145	5.4	332	7.21	24	14	95	42
20	Revathy	50	Female	61649	Type2	UTI	69	1.4	456	144	4.8	333	7.19	20	13	95	42
21	Radhakrishnan	63	Male	62806	Type2	NSTEMI	61	1.2	430	132	5.1	308	7.2	27	14	32	36
22	Venugopal	54	Male	63603	Type2	NSTEMI	54	1.2	412	132	5.2	306	7.2	26	13	70	32
23	Deveudran	60	Male	64573	Type2	Omission	59	1.2	356	138	5.6	316	7.2	26	14	95	42
24	Aruldoss	70	Male	65183	Type2	AGE	52	1.2	413	131	5.1	304	7.2	29	14	95	42
25	Alimohamed	50	Male	65488	Type2	CVA	59	1.4	412	124	3.6	287	7.2	28	14	95	42
26	Suresh	45	Male	67985	Type2	UTI	64	1.5	434	148	5.4	341	7.18	24	14	95	42

27	Santharam	54	Male	68005	Type2	CVA	56	1.3	464	140	4	322	7.2	25	12	95	42
28	Kalyani	48	Female	69200	Type2	Pneumonia	61	1.3	389	148	5.4	338	7.24	21	12	95	42
29	Elisebath	77	Female	71337	Type2	CVA	54	1.3	392	151	5.6	343	7.2	21	12	95	42
30	Devraj	43	Male	71879	Type2	Acute MI	51	1.1	312	132	5.4	300	7.1825	22	13	95	42
31	Kumeresan	17	Male	72273	Type1	Omission	78	1.1	380	128	3.9	298	7.2	28	13	356	59
32	Kumaresan	17	Male	72378	Type1	New case	81	1.3	513	135	5.8	323	6.8	21	7	49	198
33	Rajarathnam	65	Male	72410	Type2	Age	68	1.4	456	132	5.6	311	7.1825	22	14	95	42
34	Abirami	13	Female	72758	Type1	Omission	54	1.2	350	135	5.5	309	7.2	21	12	95	42
35	Shakira begam	65	Female	73947	Type2	UTI	64	1.5	346	146	5.5	332	7.2	24	14	95	42
36	Ragu	46	Male	74745	Type2	Acute MI	49	1.2	321	130	5.1	295	7.25	27	14	95	42
37	Anandhan	50	Male	75115	Type2	CVA	56	1.4	391	143	5	322	7.2	27	13	95	42
38	Gurunathan	62	Male	75238	Type2	CVA	61	1.3	346	121	5	281.2	7.21	28	15	95	42
39	Anbalagan	61	Male	75727	Type2	CVA	59	1.3	399	134	4.9	354	7.27	21	13	95	42
40	Kanniammal	65	Female	76320	Type2	CVA	64	1.4	431	148	5.6	341	7.2	22	14	95	42
41	Kavipriya	20	Female	76393	Type1	New case	59	1.3	356	140	5.4	320	7.23	22	12	95	42
42	Abdul majid	52	Male	77445	Type2	Pneumonia	59	1.2	404	122	4.8	286	7.21	25	12	95	42
43	Velu	38	Male	79883	Type2	Pneumonia	72	1.5	386	126	5	295	7.2	24	13	95	42
44	Rajeshwaran	14	Male	80015	Type1	New case	70	1.6	505	126	5.1	301	7.2	21	12	95	42
45	Yuvarai	15	Male	82326	Type1	New case	59	1.4	456	142	5	329	7.2	24	13	95	42
46	Ravi	50	Male	82783	Type2	Omission	60	1.2	382	130	5.2	301	7.2	26	13	95	42
47	Kaliyamoorthy	65	Male	84314	Type2	Pneumonia	52	1.4	290	128	5.1	290	7.3	2.4	13	95	42
48	Nitin Jose	21	Male	84399	Type1	New case	62	1.3	434	124	3.8	290	7.2	22	15	95	42
49	Panner selavam	52	Male	84692	Type2	Inadequate Insulin	62	1.3	456	138	5.4	321	7.2	26	12	95	42
50	Poosanam	64	Male	142905	Type2	Acute MI	63	1.2	430	131	5.1	306	7.2	26	13	302	152